REMARKS

The rejection of claims 1, 5-6 and 8-10 under 35 USC 103(a) as being unpatentable over Zhang et al. '981 in view of the newly cited reference Baichwal A.R., U.S. Patent 5,846,563, is respectfully traversed. In addition, the rejection of claims 19-25 as being anticipated by Murakami et al. (JP 403280854 – English Abstract), is respectfully traversed.

Claim 1 of the present application is directed to a sustained release composition of (sodium alginate:xanthan gum = 1:0.1 to 10) and a gel hydration accelerator (HPMC and propylene glycol alginate = 1:0.05 to 20), wherein the weight ration of the drug: the carrier: the gel hydration accelerator are required to be in a specified weight ratio of 1:3 to 30:0.1 to 15.

1) The technical problem addressed by Zhang is completely different from that of the present invention.

Contrary to the Examiner's allegation "that Zhang teaches a sustained-release composition for oral administration comprising nifedipine" (see page 2, last paragraph of the Office Action), Zhang is directed to an oral transmucosal delivery system which is dependent upon absorption through the mucosal tissues, which inherently involves a rapid or instant release as known to those skilled in the art.

The Examiner also alleges that "Zhang provides a mechanism of controlling drug release by controlling the dissolution and disintegration". To the contrary, Zhang teaches absorption solely through the mucosal tissue which is known to be a rapid or instant release and is not a sustained release as known to those skilled in

the art.

Zhang teaches using a solid solution wherein a dissolution agent is combined with a pharmaceutical agent at a molecular level. That is, in Zhang, to improve the solubility and stability of the drug so as to work effectively in the unique environment of the oral cavity, a limited amount of solvent is used in a relatively short period of time for drug delivery by absorption of the drug through the mucosal tissue.

The oral transmucosal delivery taught in Zhang is clearly distinguished from a general oral delivery route (i.e., gastrointestinal route) due to its much shorter onset time (i.e., the time from administration to therapeutic effect) (see column 1, lines 44-46 of Zhang). In other words, Zhang is teaching an instant release formulation as opposed to a sustained release formulation.

In view of the foregoing, those having ordinary skill in the art would not readily employ the agents disclosed in Zhang in a solid solution to achieve a sustained release formulation dependent upon a gastrointestinal delivery.

Furthermore, although various dissolution agents suggested in Zhang include all of the four (4) components of the present invention (i.e., HPMC, polypropylene glycol alginate, sodium alginate and xanthan gum) (see column 7, lines 23 to 35 of Zhang), Zhang fails to provide any guidance which would suggest to a person skilled in the art how to combine the specific combination of the four (4) agents and in what weight ratio as is required in claim 1. Claim 1 is dependent upon using the claimed weight ratios.

2) The two (2) types of the agents of the present invention, i.e., a carrier for sustained release and a gel hydration accelerator, are neither taught nor suggested in Baichwal '563.

Baichwal '563 discloses a sustained release formulation for an insoluble active ingredient comprising a drug and the following three (3) kinds of sustained release excipients:

gelling agent: xanthan gum, locust bean gum, etc.,

inert diluent: monosaccharide, disaccharide, polyhydric alcohol, etc., and

water-soluble cationic cross-linking agent: calcium sulfate, etc.

The Examiner alleges that Baichwal teaches a combination of a gelling agent and an inert diluent, i.e., a mixture of xanthan gum and locust bean gum, with or without a cross-linking agent and hydrophilic polymer, i.e., HPMC, to provide a product to which the desired active medicament (nifedipine) is thus increased based on the teaching in Baichwal in column 8, lines 19 to 27.

However, Baichwal teaches using a hydrophobic polymer, not a hydrophilic polymer.

Actually, when the formulation of Baichwal is prepared, the sustained release excipients are granulated with a solution or dispersion of a hydrophobic polymer such as ethylcellulose, acrylic and methacrylic acid esters, waxes, etc. prior to admixture of the sustained release excipients with the medicament and tableting (see column 4, lines 23 to 30 of Baichwal) in order to slow the hydration of the

gelling agent without disrupting the hydrophilic matrix (see column 3, lines 36 to 39).

Accordingly, the combination of a gelling agent and a hydrophilic polymer, which may correspond to the combination of a carrier for sustained release and a gel hydration accelerator of the present invention, is not disclosed in Baichwal.

In addition, Baichwal neither teaches nor suggests the use of sodium alginate and propylene glycol alginate.

3) The sustained release effect of the composition of the subject invention is unexpected relative to the compositions taught in Zhang and in Baichwal.

(a) The sustained release composition of the present invention is capable of releasing the drug at a constant rate following zero order kinetics for 24 hours or more, the rate being affected little by the degree of gastrointestinal motility.

(b) In contrast, Zhang does not teach or is capable of providing such sustained release of a drug since Zhang relates to an instant release formulation wherein a drug is rapidly absorbed through the oral mucosal tissues, rather than a sustained release formulation wherein a drug is absorbed in the gastrointestinal tract for a long period of time.

The fact that the formulation of Zhang aims to provide the instant release of a drug is supported by Examples 1 and 3 in Zhang, especially by the following descriptions:

The data also show faster absorption into the blood stream (tmax) (column 12, lines 60 to 61).

As with the other experiments, the data show that etomidate is absorbed at a faster rate and to greater extent (increased bioavailability) when delivered using the present invention (column 14, lines 58 to 61).

Although Baichwal is directed to a sustained release formulation, the formulation of Baichwal is entirely different from that taught in claim 1 and fails to release the drug at a constant rate following zero order kinetics for 24 hours or more in view of the data shown in Tables 3, 6, 9, 13 and 16 in Baichwal.

The argument of the Examiner regarding the claimed weight ratios of the subject invention contradicts the objective in Zhang for providing an instant release formulation by oral transmucosal delivery. Accordingly, one skilled in the art would not consider combining selected components in combination for non-oral transmucosal delivery where a sustained release of a drug at a relatively constant rate is desired following zero order kinetics for 24 hours or more. To achieve this, the weight ratios as claimed is critical. This is fully supported by the data presented in Figs. 6A to 8D and Table 3 of the subject application and as supported in the additional experimental data shown in the Declaration under Rule 312, filed on June 7, 2007.

Reconsideration and allowance of the claims pending in the application is respectfully solicited.

Respectfully submitted,

Dated: May 29, 2008

By: _____
Eugene Lieberstein
Registration No. 24,645

CUSTOMER NO.: 79681

BAKER & HOSTETLER, LLP
45 Rockefeller Plaza
New York, NY 10111
Phone: 212-589-4644

CERTIFICATE OF TRANSMISSION

I hereby certify that this Amendment is being submitted to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 via EFS-Web on May 29, 2008.

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Audrey de Souza